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Letter to the Editor | Letter to the Editor

Influence of vaccination and prior immunity on the dynamics of Omicron BA.1 and BA.2 sub-variants

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Keywords

SARS-CoV-2, Public Health, Statistical model, Omicron

Dear Editor,

The B.1.1.529 SARS-CoV-2 lineage, named Omicron, was recently divided into three lineages (BA.1, BA.2 and BA.3). BA.1 and BA.2 are much more dominant than BA.3. BA.1 could cause breakthrough infections in highly immune populations (1). Preliminary studies indicate that BA.2 can readily overcome the immunity provided by vaccination and/or infection with an earlier variant. We used data for the French city of Toulouse to evaluate the impact of the proportions of the BA.1 and BA.2 variants in positive-testing samples and the impact of vaccination on SARS-CoV-2 proliferation.

Our discretized version of a susceptible infectious and recovered (SIR)-type model has been shown well suited to studies on the spread of SARS-CoV-2 (2,3).

The model includes a diffusion/transmission coefficient R_0 that varies with the likelihood of contagion, and two reduction coefficients $\hat{c}$ and $\hat{q}$ that describe the impact of public health measures on virus transmission. Values of $\hat{c}$ and $\hat{q}$ were estimated in previous studies (2,3). It also takes into

account a parameter p_1 describing the proportion of the BA_1 variant in urban Toulouse, and a similar parameter p_2 for the BA_2 variant; there are also vaccine/immunity efficacy coefficients $\widehat{\iota_1}$ and $\widehat{\iota_2}$ indicating the weight of each variant in the number of new infections. The model predicts how the SARS-CoV-2 virus would have evolved and projects the daily percentage of new positive cases (see Supplementary materials S1).

We set $R_0(D) = 5.9$ for the Delta variant at its peak, based on WHO international data (4). First elements showed that $R_0(BA_1)$ could reach 10 (5). We estimated the initial model settings using data collected by Toulouse Virology Laboratory (Table 1).

The nucleic acids in nasopharyngeal swab samples collected at Toulouse University Hospital were extracted with the MGI extraction system and tested using the ThermoFisher TaqPath RT-PCR assay. All positive nasopharyngeal samples with a cycle threshold (Ct) value below 30 (N gene) were tested using the ID solutions screening system for mutations K417N, L452R and E484K. The Omicron BA.1 variant was identified based on TaqPath S gene target failure (SGTF) or S gene target late (SGTL) detection profiles plus the presence of the K417N mutation. The Omicron BA.2 variant was identified based on TaqPath non-SGTF/SGTL detection profiles plus the presence of the K417N mutation. The results for a subset of 1080 positive specimens tested with our VOC screening strategy and those obtained by genome sequencing using Pacific Biosciences Technology (6) were 100% concordant.

In addition to barrier measures, the local authorities decided to make mask wearing compulsory in the Toulouse area from November 24, 2021 (week 47) as this protective measure had been shown to reduce SARS-CoV-2 circulation among Toulouse inhabitants by 27% (3). The BA.1 variant was the major variant (> 90%) in the Toulouse area from January 1 to February 1 (weeks 1-4, Table 1). The parameters of its R_0 (see Methods; $R_0 = 10$) predicted that the percentage of new positive cases during this period would be 20.9% if 69.8% of the fully vaccinated population was as protected against BA.1 infection as they were against Delta: <88% (7) (Figure 1A). The vaccine/immunity efficacy coefficient $\widehat{\iota_1}$ was about 23% after correction based on the observed data (Equation 1,

Supplementary S1) (Figure 1C). The proportion, p_2, of BA.2 variant increased from 5.5% at the end of January 2022 to 39.9% on February 21, 2022 (Table 1). The rate of positive RT-PCR tests should have doubled between February 1 and 21 if the vaccine/immunity efficacy for BA.2 is close to 23%, the same as that for BA.1 (Figure 1B). However the percentage of positive RT-PCR tests decreased from 44% on February 4 to 19.6% on February 21 (weeks 5-7, Table 1). Correcting the model parameters to bring the predicted data in line with the observed data (Equation 2, Supplementary S1) gave a vaccine/immunity coefficient of 92.8% (Figure 1C).

The rapid proliferation of BA.1 was different from that of the Delta variant, which became the dominant strain in the summer months, when health measures were relaxed and vaccination coverage lower. This indicates the great capacity of the BA.1 variant to evade antibodies produced in response to infection with an earlier strain of virus and antibodies generated by vaccination. We showed that the Omicron BA.1 variant was more contagious than the Delta variant because of vaccine escape resulting from the spike mutations that alter virus neutralization rather than because of greater virus shedding in the nasopharynx (8). The "BA.1 wave" seems to induce significant natural immunity against the BA.2 variant. The slowdown in the spread of the SARS-CoV-2 virus could also be due to the vaccine booster campaign that started at the beginning of January 2022 when about 76% of those who were primo-vaccinated had been given 3 doses by mid-February 2022. We could not distinguish between the influence of a booster vaccination and the immunity conferred by a BA.1 infection on the spread of BA.2, because the two events were confounded. These results agree with those showing that BA.2 and BA.1 are similarly able to resist the neutralizing antibodies of people who had been vaccinated or previously infected (9). A slight difference in neutralizing capacity against Omicron BA.1 and BA.2 of natural or vaccine antibodies could explain a growth advantage of BA.2 over BA.1. In a Danish study, unvaccinated individuals, like vaccinated individuals, were more susceptible to BA.2 infection than to BA.1 infection indicating that viral properties other than immune evasion could also play a role in the growth advantage of BA.2 (10).

We conclude that the increase in the proportion of BA.2 has not led to a faster spread of the virus; which seems to indicate that the immunity induced by BA.1 infection is effective against BA.2. Further studies are needed to determine the contributions of the vaccine booster and a BA.1 infection to protection against BA.2.

Declaration of Competing Interest

The authors have no conflict of interest to declare.

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Figure 1: Daily dynamics of SARS-CoV-2 infection, July 21, 2020 to February 21, 2022
A. Assuming that the Omicron BA.1 sub-variant is as sensitive as Delta to vaccination/previous immunity
B. Assuming that the Omicron BA.2 sub-variant is as sensitive as BA.1 to vaccination/previous immunity
C. Real daily dynamics of SARS-CoV-2 infection, July 21, 2020 to February 21, 2022

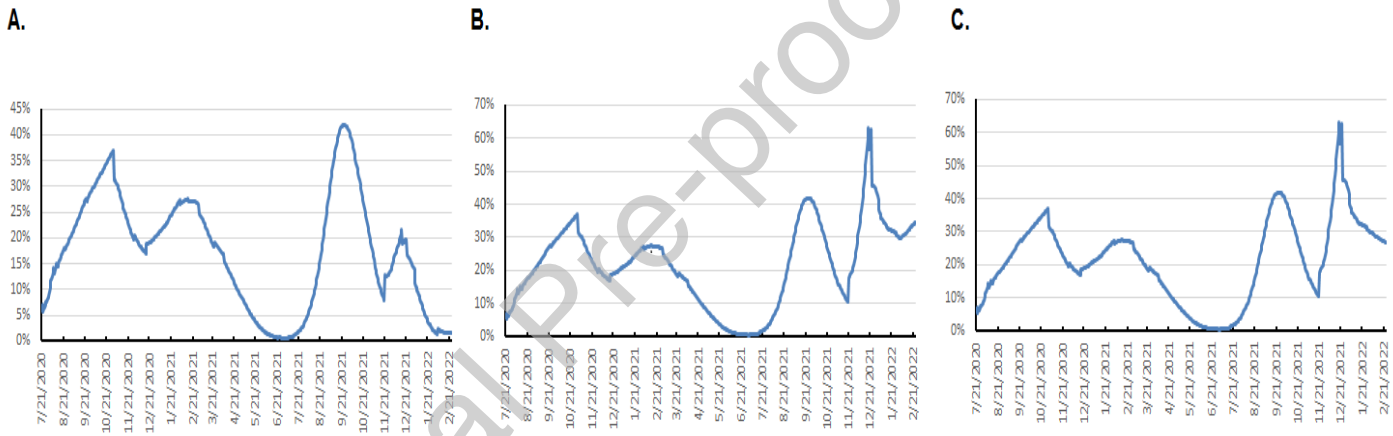

Table 1: Model initial parameters

		Weeks 2021																	Weeks 2022						
		36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	1	2	3	4	5	6	7
Variant (%)	Delta	98.5	91.8	87.5	100	100	100	100	100	98.6	100	86.9	97.4	99.5	99.4	90.1	45.1	17.9	2.3	1.2	0.2	0.2	0.1	0	0
	BA.1	0	0	0	0	0	0	0	0	0	0	0	0	0.2	0.6	9.9	54.7	82.1	97.4	97	97.9	94.3	87.7	77.3	60.1
	BA.2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.3	1.8	1.9	5.5	12.3	22.7	39.9
	Non Delta/ Non Omicron	1.5	8.2	12.5	0	0	0	0	0	1.4	0	13.1	2.6	0.2	0	0	0.2	0	0	0	0	0	0	0	0
Tests	Total number	1535	1361	1107	947	877	1025	1250	1556	1573	1709	1584	2565	3526	4292	4778	5506	6664	8998	7622	6049	3794	2368	1619	1921
	Positive (%)	5.9%	4.8%	4.1%	4.8%	2.0%	2.9%	3.4%	3.4%	5.3%	5.1%	7.1%	14.5%	16.7%	16.5%	14.3%	21.8%	33.1%	38.4%	42.1%	47.5%	41.6%	32.1%	27.7%	19.6%